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Abstract: Introduction: In Parkinson's disease (PD), neuropsychiatric symptoms (NPS) can be particularly burdensome for caregivers. The main goal of this study was to assess the impact of NPS, assessed by means of a new specific scale, on caregiver burden. Methods: A sample of 584 pairs of PD patients and their primary caregivers was studied. Patients' NPS were measured with the Scale for Evaluation of Neuropsychiatric Disorders in PD (SEND-PD), and the Zarit Caregiver Burden Inventory was used to quantify caregiver burden. Three linear regression models were built to check factors associated with caregiver burden, one for the total sample and two for subgroups stratified by the presence of dementia. Results: The most prevalent SEND-PD dimensions were mood/apathy (87.4%), followed by psychotic symptoms (48.5%) and impulse control disorders (26.5%). Patients with dementia (n=94; 16.15% of sample) consistently presented more NPS than patients without dementia ($p<0.001$). On linear regression models, the main determinants of caregiver burden (for the total sample and the sample of patients without dementia) were SEND-PD dimensions mood/apathy and psychosis, PD-related disability and disease duration. For patients with dementia, the only significant caregiver burden determinants were SEND-PD psychosis and mood/apathy subscale scores. Conclusions: NPS in PD are highly associated with and are determinants of caregiver burden, and are more prevalent and burdensome in patients with dementia. Detailed assessment and specific interventions aimed at NPS could alleviate caregiver burden.


Author Declaration

Parkinsonism & Related Disorders is committed to proper scientific conduct and the protection of animal and human research subjects. Submission of this manuscript implies compliance with the following ethical requirements. Please affirm that you are representing all of the authors in stating compliance with these policies by checking the box at the end of this section.

1. Studies with human subjects must have been conducted in accordance with the Declaration of Helsinki. All persons must have provided informed consent prior to being included in the study.
2. Studies with animal subjects must have been conducted in accordance with the Guide for the Care and Use of Laboratory Subjects as adopted by the US National Institutes of Health and/or according to the requirements of all applicable local, national and international standards.
3. Protocols with animal or human subjects must have been approved by the relevant local committee(s) charged with ensuring subject protection. Studies that entail pain or distress will be assessed in terms of the balance between the distress inflicted and the likelihood of benefit.
4. The authors declare that the manuscript is original, that it is not being considered for publication elsewhere, and that it will not be submitted elsewhere while still under consideration for Parkinsonism & Related Disorders or after it has been accepted by Parkinsonism & Related Disorders.
5. All authors have seen and approved the manuscript in the form submitted to the journal. The authors declare that they have conformed to the highest standards of ethical conduct in the submission of accurate data and that they acknowledge the work of others when applicable.
6. All sources of financial support for the work have been declared in the Acknowledgements section of the manuscript. Any additional conflicts of interest must also be declared. Please include declarations of any consultancy or research funding received from relevant companies from three years prior to performance of the research until the time of manuscript submission. If the research is supported by internal funds, that should be stated as well.

To indicate compliance with the preceding declaration and that you have obtained agreement from all of the authors of this paper to declare their compliance as well, please place an x here: X

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Prof. Pfeiffer and Prof. Wszolek
Editors-in-Chief
Parkinsonism and Related Disorders

November 6th, 2014

Dear Professors,

Please, find attached our manuscript “Neuropsychiatric symptoms and caregiver’s burden in Parkinson’s disease” to be considered for publication as a full length article in the prestigious journal that you head.

As first and corresponding author, I declare that all authors expressed their conformity with the current version, this is an original paper that has not been published previously, and it is not in consideration by any other journal.

Yours sincerely,



Dr Pablo Martinez-Martin

On behalf of all co-authors

Highlights

- In Parkinson's disease (PD), neuropsychiatric symptoms (NPS) notably increase caregiver burden
- In this study, NPS were assessed with the Scale for Evaluation of Neuropsychiatric Disorders in PD
- PD patients with dementia experience more NPS, a fact adding extra burden to caregivers
- NPS were the main determinant of caregiver burden, both in PD patients with and without dementia

Neuropsychiatric symptoms and caregiver’s burden in Parkinson’s disease

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Abstract

Introduction: In Parkinson's disease (PD), neuropsychiatric symptoms (NPS) can be particularly burdensome for caregivers. The main goal of this study was to assess the impact of NPS, assessed by means of a new specific scale, on caregiver burden.

Methods: A sample of 584 pairs of PD patients and their primary caregivers was studied. Patients' NPS were measured with the Scale for Evaluation of Neuropsychiatric Disorders in PD (SEND-PD), and the Zarit Caregiver Burden Inventory was used to quantify caregiver burden. Three linear regression models were built to check factors associated with caregiver burden, one for the total sample and two for subgroups stratified by the presence of dementia.

Results: The most prevalent SEND-PD dimensions were mood/apathy (87.4%), followed by psychotic symptoms (48.5%) and impulse control disorders (26.5%). Patients with dementia (n=94; 16.15% of sample) consistently presented more NPS than patients without dementia ($p<0.001$). On linear regression models, the main determinants of caregiver burden (for the total sample and the sample of patients without dementia) were SEND-PD dimensions mood/apathy and psychosis, PD-related disability and disease duration. For patients with dementia, the only significant caregiver burden determinants were SEND-PD psychosis and mood/apathy subscale scores.

Conclusions: NPS in PD are highly associated with and are determinants of caregiver burden, and are more prevalent and burdensome in patients with dementia. Detailed assessment and specific interventions aimed at NPS could alleviate caregiver burden.

Keywords: Parkinson's disease, caregiver burden, neuropsychiatric symptoms

Highlights

- In Parkinson's disease (PD), neuropsychiatric symptoms (NPS) notably increase caregiver burden
- In this study, NPS were assessed with the Scale for Evaluation of Neuropsychiatric Disorders in PD
- PD patients with dementia experience more NPS, a fact adding extra burden to caregivers
- NPS were the main determinant of caregiver burden, both in PD patients with and without dementia

INTRODUCTION

Parkinson's disease (PD) is a chronic, neurodegenerative condition that significantly impacts on patients and on those who look after them on a daily basis. As their health status deteriorates, patients need progressively more assistance to perform their activities of daily living. Caregiving is time consuming and demanding. Its negative impact on the caregiver's health, social life and financial situation is summarized in the construct of "caregiver burden" [1].

Factors influencing caregiver burden are related to caregiver and patient characteristics, including PD manifestations and consequences [2]. Patients differ substantially on their degree of disability, motor and non-motor symptom profiles, and complications of therapy [3], all of which may have a differential impact on caregiver burden. Neuropsychiatric symptoms (NPS), such as anxiety, depression, apathy, mental fatigue, psychosis, and impulse control disorders (ICDs) are highly prevalent, affecting up to 60-80% of patients with PD [4]. Although NPS can occur in PD patients without dementia [5], cognitive impairment is a correlate of most of these disturbances and, as a whole, NPS are more frequent in patients with dementia. Their co-occurrence highly increases caregivers burden [6–8]. Both, presence and severity of NPS are associated with increased caregiver burden [6,9] and, by modality, psychotic symptoms are especially important. They are disruptive, significantly increase caregiver burden [6,9] and can lead to institutionalization of PD patients [10,11].

The present study aims to assess how NPS, measured with the disease-specific Scale for Evaluation of Neuropsychiatric Disorders in PD (SEND-PD) [12], impact on caregiver burden. We hypothesized that: 1) There is a significant relationship between caregiver burden and NPS; 2) PD patients with dementia present more NPS than PD patients without dementia; 3) Caregivers will suffer more burden when patients

experience NPS with dementia; 4) NPS are the main determinants of caregiver burden both in PD patients with and without dementia.

METHODS

Sample

The sample consisted of 584 pairs of consecutive patients and their main caregivers from the SEND-PD validation study [12]. Patients were included if: PD diagnosis was made by a neurologist according to internationally recognized diagnostic criteria [13]; caregiver was present during the visit; and patients or their legal representative signed informed consent. Patients who did not meet all inclusion criteria or who had a condition that could hamper the assessment were excluded.

The caregiver was defined as “any person who, without being a professional or belonging to a social support network, usually lives with the patient and, in some way, is directly implicated in the patient’s care or is directly affected by the patient’s health problem” [2]. Caregiver inclusion criteria were: age 18 years or older, ability to complete self-administered questionnaires in Spanish, and willingness to sign informed consent.

Ethical Approval

The study was approved by the institutional review boards of the Carlos III Institute of Health and Alzheimer’s Disease Research Unit, CIEN Foundation and was reported to the Spanish Medicines Agency [12]. Patients or their legal representative signed informed consent.

Assessments

The following evaluations were carried out: Hoehn & Yahr staging (HY) [14] and Clinical Impression of Severity Index for PD (CISI-PD) [15]; Scales for Outcomes in PD-Motor (SCOPA-Motor) [16]; Mini-Mental State Examination (MMSE) [17], and the Pill Questionnaire and Lexical Fluency, according to the diagnostic procedures for PD dementia [18]. The Scale for Evaluation of Neuropsychiatric Disorders in PD (SEND-PD) was used to assess the presence of NPS [12].

A clinical judgment on the dementia status of each patient (normal, cognitive impairment without dementia, or dementia and degree of severity), based on the patient's medical record, interview with the patient and caregiver, and assessments, was recorded. This question was used to group patients with or without dementia.

The SEND-PD is a rater-based scale specifically developed to assess the severity of most relevant NPS found in PD. It is informed by the patients or caregivers if patients can not answer the questions properly. Its 12 items are grouped in three dimensions: psychotic symptoms (4 items), mood/apathy (5), and ICD and related behaviors (3). Items are scored from 0 (not present) to 4 (very severe) and a total sum score is obtained for each domain. It shows satisfactory psychometric properties [12].

Caregiver burden was assessed with the Zarit Caregiver Burden Inventory (ZCBI) [19], a 22-item measure assessing the impact of the patient's disease or disability on the caregiver's physical, emotional, social and financial situation. Items are scored from 0 (never) to 4 (nearly always), with a maximum total score of 88 indicating the highest level of caregiver burden.

Socio-demographic data from patients and caregivers were collected. Levodopa equivalent daily doses (LEDD) were calculated [20].

Data analysis

Descriptive statistics were used for socio-demographic and clinical variables. For NPS prevalence, the percentage of patients scoring >0 (presence of the symptom) in each SEND-PD item and domain was calculated for the total sample and by dementia status (patients with and without dementia).

To analyze the relationship between ZCBI and the other variables, Spearman's correlation coefficients were determined for the total sample and dementia status groups. Coefficients of 0.35-0.59 were deemed as moderate, while coefficients ≥ 0.60 were considered high [21].

ZCBI mean values were calculated in the sample broken down by groups of interest: patients' and caregivers' sex and age, education level, relationship, disease duration, HY, cognitive status, and presence of NPS as per SEND-PD subscales. Mann-Whitney and Kruskal-Wallis tests were used to ascertain the differences between groups. In addition, specific comparisons of caregiver burden were determined for patients with NPS according to their dementia status (Mann-Whitney tests).

A linear regression model was built using ZCBI as the dependent variable and disease duration, disability, NPS and dementia status as independent variables. Similar models, removing dementia status as predictor, were then repeated for the groups by dementia status. Linear regression assumptions were previously checked.

RESULTS

Table 1 presents patients and caregivers description. Table 2 displays the prevalence of NPS assessed by the SEND-PD. The SEND-PD was responded by patients (87.03%), caregivers (12.59%) or both (0.38%).

Patients with dementia (n=94; 16.15%) consistently presented more NPS than patients without dementia ($p<0.007$) in all domains (Table 2). For patients with dementia, the most prevalent symptom was apathy. For patients without dementia, the most prevalent symptom was depression. For the entire sample, the most prevalent symptoms were depression and anxiety

ZCBI score in total sample was moderately associated with CISI-PD ($r_s=0.56$, $p<0.001$), SCOPA-Motor ($r_s=0.56$, $p<0.001$), and PIGD scores ($r_s=0.53$, $p<0.001$). A moderate association was also observed with HY stage ($r_s=0.46$, $p<0.001$) and MMSE ($r_s=-0.35$, $p<0.001$). ZCBI score correlated 0.32 to 0.53 with the SEND-PD dimensions ($p<0.001$) in the total sample. In the group without dementia, ZCBI correlated 0.34 with SEND-PD Psychotic, 0.44 with Mood/Apathy and 0.25 with Impulse Control Disorders ($p<0.001$), while in the group with dementia, correlation coefficients with SEND-PD subscales were 0.51, 0.34, and 0.32, respectively ($p<0.001$).

Caregivers of patients with NPS reported significantly higher burden than caregivers of patients without symptoms ($p<0.001$; Table 3). Comparing the group of patients with NPS by dementia status, caregivers of patients with dementia reported a significantly higher burden than those without dementia ($p<0.001$ for the three SEND-PD subscales; Table 3).

Linear regression models (Table 4) indicate that the SEND-PD dimensions mood/apathy (standardized $\beta=0.28$) and psychosis ($\beta=0.18$); disability ($\beta=0.21$) and disease duration ($\beta=0.11$) were significant determinants of ZCBI score for the entire cohort.

Caregiver burden of patients without dementia was associated with higher SEND-PD mood/apathy ($\beta=0.28$) and psychosis scores ($\beta=0.15$), higher disability ($\beta=0.21$) and longer disease duration ($\beta=0.13$). For patients with dementia, the only

significant determinants were SEND-PD psychosis ($\beta=0.31$) and mood/apathy scores ($\beta= 0.28$).

DISCUSSION

In PD, motor symptoms and complications are well established factors that are intrusive to daily life and increase caregiver burden. The aim of this study was to assess the impact of NPS and dementia on caregivers' burden, using a recently developed PD-specific scale for the assessment of NPS, the SEND-PD [12].

In our cohort, caregivers were mostly middle-aged women who took care of a male patient/spouse, a profile coincident with most studies on PD caregivers [5,22]. In the present study, ZCBI scores were associated with SEND-PD dimensions, thus confirming the first hypothesis on a relationship between caregiver burden and presence and severity of NPS. Also, and in agreement with a previous study [5], other PD aspects such as motor impairment, disease severity and PD subtype, were also related to caregiver burden. Interestingly, the correlation between caregivers' burden and psychotic symptoms was higher in PD patients with dementia than in those with normal cognition. PD patients with dementia have a greater prevalence of psychotic symptoms than patients without dementia, as hypothesized in this study, and this fact increases caregiver burden [23,24].

Different profiles of NPS according to cognitive status were observed in this study: while PD patients with normal cognitive function had more depression and anxiety, PD patients with dementia showed higher percentages of apathy/lack of initiative and mental fatigue. For the entire sample, the most prevalent NPS were those pertaining to the mood/apathy domain, followed by psychotic symptoms. These results are in line with previous studies [4,8] and highlight the need for carrying out complete

neuropsychiatric assessments of PD patients in clinical practice, and for evaluating the effects that PD treatments may have on NPS [8].

Caregivers reported significantly more burden when patients experienced NPS and dementia, suggesting a synergetic effect of dementia and NPS on caregiver burden. This confirms our third hypothesis and is congruent with previously reported increased caregiver burden in patients with dementia, compared with those without dementia [23].

Our study identified mood/apathy and psychosis as significant determinants of caregiver burden. Disability and disease duration also contributed significantly to caregiver burden in patients without dementia. ICD symptoms were not associated with caregiver burden when controlling for other factors. This confirms our fourth hypothesis that NPS are main determinants of caregiver burden, particularly mood/apathy and psychosis, while ICDs may play a lesser role. This is consistent with a recent study reporting that although caregivers of patients with ICD displayed more burden than caregivers of patients without ICD, the association between ICD symptoms and caregiver burden was low [25]. In another study, cognitive behavioral therapy for patient's ICD did not alleviate caregiver burden [26].

Previous studies have documented the significant impact of the patient's mood/apathy [25], psychotic symptoms [4], disability [9,22] and disease duration [27] on caregiver burden [28]. Screening for these factors, and specifically patient's NPS and dementia, may help identify caregivers who could benefit from intervention strategies such as group support or respite care [29].

According to the stress-appraisal model of caregiver wellbeing, behavioral problems (including NPS), cognitive impairment (dementia in our study) and functional dependency are primary stressors that have a direct impact on caregiver burden, as well as an indirect effect through mediator variables [30,31]. Our results indicate that the

contribution of NPS and disability to caregiver burden is different for patients with and without dementia. In the group of patients with dementia, the only significant determinants of caregiver burden were mood/apathy and psychotic symptoms. Further studies are needed to investigate if dementia could also be acting in moderating the relationship between primary stressors and caregiver burden.

Our study has some limitations, such as the convenience sample used. However, its relatively large size and patients characteristics similar to other studies allow confidence in the consistency of the reported results. Furthermore, the cross-sectional design prevents from making causal inferences. Information from patients in more advanced stages or with dementia was obtained through their caregivers, which may bias the data. Finally, further studies are needed that explore more deeply what characteristics of caregivers might influence its burden.

In conclusion, caregivers of patients with PD are subjected to a variety of problems that influence their health, social life, financial situation, and quality of life. What this study adds is the use of a new specific instrument for assessment of NPS (SEND-PD), which enabled us to confirm that these disorders were closely associated with caregiver burden, were more prevalent and burdensome in patients with dementia, and performed as the main determinants of the caregiver burden in this study.

Financial Disclosures

Pablo Martinez-Martin received honoraria from speaking engagements at scientific meetings of Abbvie and Teva, and from serving in a scientific advisory board of Abbvie; grants from Carlos III Institute of Health, IMSERSO, Reina Sofia Foundation, and Michael J. Fox Foundation. He is Chair of the IPMDS Committee for Development of Rating Scales. His employment is at Carlos III Institute of Health.

Carmen Rodríguez-Blázquez has nothing to disclose. Her employment is at Carlos III Institute of Health.

Maria João Forjaz has nothing to disclose. Her employment is at Carlos III Institute of Health.

Belén Frades-Payo has nothing to disclose. Her employment is at Alzheimer Center Reina Sofia Foundation, Carlos III Institute of Health.

Luis Agüera-Ortiz has nothing to disclose. His employment is at Alzheimer Center Reina Sofia Foundation, Carlos III Institute of Health.

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Ana Riesco has nothing to disclose.

Monica M. Kurtis received personal fees from UCB Pharma for lectures. She is employed at Hospital Ruber Internacional.

Kallol Ray Chaudhuri has received funding from Parkinson's UK, NIHR, UCB, European Union and has received honorarium from UCB, Abbott, Britannia, US Worldmeds, Otsuka pharmaceuticals in the last 3 years and acted as a consultant for Abbvie, UCB, Britannia. His employment is at King's College Hospital.

Authors' Roles

1 – Conception and Design: Pablo Martinez-Martin. Acquisition of data: Belén Frades-Payo, Luis Agüera-Ortiz. Analysis of data: Pablo Martinez-Martin, Carmen Rodriguez-Blazquez, Maria João Forjaz, Ana Riesco. Interpretation of data: Pablo Martinez-Martin, Carmen Rodriguez-Blazquez, Maria João Forjaz.

2 – Drafting of the manuscript: Pablo Martinez-Martin, Carmen Rodriguez-Blazquez, Maria João Forjaz. Critical review of the draft: All the coauthors.

3 – Final approval of the submitted manuscript: All the coauthors.

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Table 1. Sociodemographic and clinical variables of patients and caregivers

Table 2. Prevalence of neuropsychiatric symptoms (SEND-PD) for patients with and without dementia

Table 3. Zarit values in the sample broken down by groups of interest.

Table 4. Linear regression models for Zarit as dependent variable.

Table 1. Sociodemographic and clinical variables of patients and caregivers

Patients					
Variable		n	%	Variable	SD
Sex	Men	336	58.43	Age	70.75
	Women	239	41.57	Age at PD onset	62.76
Education	None	89	15.37	PD duration	8.07
	Primary	301	51.99	LEDD	201.87
	High school	124	21.42	DA-Agonist LEDD	683.15
	University	65	11.23	SCOPA-MEx	12.48
Work	Retired	355	61.5	SCOPA-ADL	6.77
	Housewives	107	18.5	SCOPA-MComp	2.31
	Employed	33	5.7	SCOPA-Motor total	21.55
	Other	82	14.3	MMSE	26.01
HY	1	133	22.81	CISI-PD	8.65
	2	268	45.97	SEND-PD:	
	3	104	17.84	- Psychotic	1.33
	4	62	10.63	- Mood/apathy	4.49
	5	16	2.74	- ICD	0.57
Caregivers					
Variable		n	%	Variable	SD
Sex	Men	166	29.54	Age	59.62
	Women	396	70.46	Zarit	21.87
Relationship	Spouse	349	61.23		
	Children	168	29.47		
	Other	53	9.3		

N: number; M: mean; SD: standard deviation; HY: Hoehn & Yahr Staging; PD: Parkinson's disease; LEDD: levodopa equivalent daily dose; DA-Agonist: Dopamine-agonist. SCOPA: Scales for Outcomes in Parkinson's Disease; MEx: Motor exploration; ADL: Activities of daily living; MComp: Motor complications; MMSE: Mini-mental Status Examination; CISI-PD: Clinical Impression of Severity Index for Parkinson's Disease; SEND-PD: Scale for Evaluation of Neuropsychiatric Disorders in Parkinson's Disease; ICD: Impulse control disorders.

Table 2. Prevalence of neuropsychiatric symptoms (SEND-PD) for patients with and without dementia

	Prevalence*			
	Total	PD-No dementia (n=488)	PD Dementia (n=94)	p**
1. Irritability/Aggressiveness	38.4	33.4	63.8	<0.001
2. Delusions	17.6	11.1	51.1	<0.001
3. Misidentification	20.7	12.3	63.8	<0.001
4. Hallucinations	22.8	15.8	58.5	<0.001
SEND-PD Psychotic symptoms	48.5	41.6	84.0	<0.001
5. Social/Verbal withdrawn	55.3	49.8	83.0	<0.001
6. Apathy/Lack initiative	54.8	48.0	90.4	<0.001
7. Mental fatigue	57.5	51.4	89.4	<0.001
8. Depression	65.6	63.1	77.7	0.007
9. Anxiety	64.7	62.1	77.7	0.004
SEND-PD Mood/Apathy	87.3	85.7	95.7	0.007
10. Hobbyism/punding	18.3	13.9	40.4	<0.001
11. Poor impulse control	18.2	15.2	33.0	<0.001
12. Abuse of medication	6.9	4.9	16.0	<0.001
SEND-PD Impulse control disorders	26.5	22.5	46.8	<0.001
Patients with NPS	89.6	87.9	97.9	<0.001

* Percentage of patients with SEND-PD Positive answer

** Chi-squared

PD: Parkinson's disease; SEND-PD: Scale for Evaluation of Neuropsychiatric Disorders in Parkinson's Disease; NPS: neuropsychiatric symptoms.

Table 3. Zarit values in the sample broken down by groups of interest.

Variable	Levels	N*	Mean	SD	p
Total sample					
SEND-PD Psychotic	No (0)	298	15.45	12.09	<0.001 (MW)
	Yes (≥1)	274	28.86	17.96	
SEND-PD Mood/Apathy	No (0)	74	10.09	9.63	<0.001 (MW)
	Yes (≥1)	498	23.62	16.70	
SEND-PD IC disorders	No (0)	421	18.89	15.18	<0.001 (MW)
	Yes (≥1)	151	30.19	17.56	
PD Dementia ^a	No	477	19.21	14.93	<0.001 (MW)
	Yes	93	35.82	17.78	
Dementia severity	No dementia	477	19.21	14.93	<0.001 (KW)
	Mild	46	30.93	17.77	
	Moderate	37	37.86	16.07	
	Severe	10	50.70	15.33	
Patients with NPS					
SEND-PD Psychotic	No PD-Dementia	195	24.80	16.713	<0.001 (MW)
	PD-Dementia	78	39.38	16.595	
SEND-PD Mood/Apathy	No PD-Dementia	407	20.75	15.126	<0.001 (MW)
	PD-Dementia	89	37.12	17.034	
SEND-PD IC disorders	No PD-Dementia	106	25.89	16.711	<0.001 (MW)
	PD-Dementia	44	41.25	14.205	

SD: standard deviation; SEND-PD: Scale for Evaluation of Neuropsychiatric Disorders in Parkinson's Disease; NPS: neuropsychiatric symptoms; PD-Dementia: Parkinson's disease with dementia; MW: Mann-Whitney test; KW: Kruskal-Wallis test.

^a Clinical judgment on dementia (yes/no).

* Numbers that do not sum 584 are due to missing data

Table4. Linear regression models for Zarit as dependent variable.

	Total sample*		PD-No dementia (n=477)		PD-Dementia (n=93)	
	Standardized beta	p	Standardized beta	p	Standardized beta	p
SEND-PD Mood/apathy	0.284	<0.001	0.281	<0.001	0.277	0.011
CISI-PD Disability	0.213	<0.001	0.213	<0.001	--	--
SEND-PD Psychosis	0.184	<0.001	0.145	0.002	0.315	0.004
Disease duration	0.112	0.003	0.132	0.002	--	--
R Squared	0.38		0.30		0.25	

Independent variables in all models: disease duration, CISI-PD Disability item, and the SEND-PD subscales (mood/apathy, psychosis and impulse control disorders). Empty cells mean non-significant variables.

* Also includes the variable “clinical judgment on dementia”, which was not significant.